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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,797	02/21/2002	Romulus Kimbro Brazzell	OP/4-31881A	9942

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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/080,797	BRAZZELL ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 13 February 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on *13 February 2006*. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: _____.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Jon Eric Angell, Ph.D.

Continuation of 11. does NOT place the application in condition for allowance because: Applicants have submitted an affadavit and other evidence (i.e., references) after a final rejection in response to the rejection of claims under 35 U.S.C. 102(b) and 35 U.S.C. 103(a) based on WO 99/26480. It is respectfully pointed out that the rejection of claims based on the teachings of the WO 99/26480 reference were set forth prior to the final office action mailed 8/8/2005 (e.g., see the non-final action mailed on 3/14/2005). However, Applicants did not submit the affidavit and other evidence until after the final rejection. Furthermore, Applicants have not provided good and sufficient reasons why the affidavit and other evidence is necessary and was not earlier presented. As such, the affidavit and other evidence will not be entered and Applicants arguments based on the evidence that has not been entered will not be considered.

With respect to Applicants arguments that do not rely on the newly submitted evidence, it is respectfully pointed out that the Arguments are esssentially the same as the arguments submitted on 5/23/2005, which were addressed in the final office action mailed 8/8/2005. Specifically, Applicants argue that the WO 99/26480 document does not provide a written description or enabling disclosure for direct administration of an endostatin expressing vector to the eye to obtain an antiangiogenic effect as is claimed in the instant application. The Applicants also argue that no particular teaching of how to deliver the vector to the eye is provided in WO 99/26480. Applicants also focus on the working examples of the WO 99/26480 and specifically assert that "There is no teaching of transferring endostatin alone for a non-cancer treatment of the eye." Applicants point out that the WO 99/26480 document has not matured into a patent and should not be given a presumption of enablement.

In response to Applicants' arguments, it is respectfully pointed out that claim 33 of the WO 99/26480 reference explicilty states, "Use of a nucleic acid molecule which expresses in said patient an anti-angiogenic polypeptide selected from the group consisting of... human endostatin, mouse endostatin...in the preparation of a medicament for treating a human patient suffering from diabetic retinopathy, wherein expression of the anti-angiogenic polypeptide in the patient inhibits angiogenesis in the vicinity of the retina." Furthermore, page 2 (last full paragraph) of the WO 99/26480 document clearly teaches ex vivo and in vivo methods and identifies in vivo therapy as a preferred embodiment. WO 99/26480 also indicates that methods preferably involve delivery of the angiogenesis inhibiting polypeptide using a viral vector or plasmid which can be administered so that cells of the patient in the vicinity of the target site are infected or transfected with the nucleic acid encoding the angiogenic-inhibiting polypeptide. Furthermore, like the instant application, the WO 99/26480 document teaches in detail a number of different viral vectors that can be used to deliver and express the therapeutic endostatin protein (e.g., see page 5). The WO document indicates that the term "a gene therapy vector" is meant to mean a vector useful for gene therapy and can be a virus, plasmid or phage (see page 5). The WO 99/26480 document teaches, "preferred vectors include, e.g., retroviral vectors, adenoviral vectors, adeno-associated vectors, herpes virus vectors, Similiki Forest Virus-based vectors, Human Immunodeficiency Virus, Simian Immunodeficiency virus, and non-viral plasmids" (see page 5). Additionally, page 9 of the WO 99/26480 document teaches, in detail, a preferred embodiment in constructing a gene therapy vector that is sufficient for use in the treatment of angiogenesis in vivo. WO 99/26480 also explicitly teaches that the eye is a specific target for the delivery of the therapeutic nucleic acid (e.g., see page 14, lines 1-15). Therefore, WO 99/26480 teaches (i.e., provides a written description) each and every element of the claims rejected under 35 U.S.C. 102(b).

With respect to Applicants arguments that the WO 99/26480 document does not provide an enabling disclosure for the claimed method, it is noted that case law states that anticipation does not require the actual creation or reduction to practice of the prior art subject matter; anticipation requires only an enabling disclosure. (In re Donohue, 766 F.2d 531, 533 [226 USPQ 619] (Fed. Cir. 1985)). A reference may enable one of skill in the art to make and use a compound even if the author or inventor did not actually make or reduce to practice that subject matter. (Bristol-Myers, 246 F.3d at 1379; see also In re Donohue, 766 F.2d at 533).

It is acknowledged that the WO 99/26480 document does not disclose a working example for the indicated method. However, in view of the state of the prior art with respect to gene therapy of the eye as well as the state of the art with respect to using endostatin as an anti-angiogenic factor in gene therapy, the WO 99/26480 document does provide a sufficient disclosure to enable the indicated method.

With respect to the rejection of claims under 35 USC 103, Applicants argue that since all of the rejections are based on the teachings of LeBoulch (WO 99/26480), and since the WO 99/26480 document does not anticipate or enable the base claims for the reasons indicated above, then the rejections are improper (e.g., see pages 4-6 of the response filed 5/23/2005). Furthermore with respect to the rejection of claims as being obvious over WO 99/26480 in view of Keshet et al. and further in view of Otani et al., Applicants argue that the secondary references do not cure the deficiencies of WO 99/26480.

In response, the Examiner disagrees that the WO 99/26480 document does not anticipate or enable the claimed method, for the reasons indicated above. Furthermore, with respect to Applicants arguments regarding the rejection based on WO 99/26480 in view of Keshet et al. and further in view of Otani et al., the Applicants appear to be arguing against the references individually. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Therefore, Applicants arguments are not persuasive.